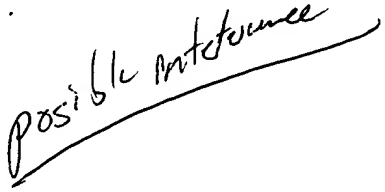
DOCUMENT NUMBER: 98214875 PubMed ID: 9554256
TITLE: **Adjuvants** and delivery systems for **viral vaccines**--mechanisms and potential.
AUTHOR: Jennings R; Simms J R; Heath A W
CORPORATE SOURCE: Division of Molecular and Genetic Medicine, University of Sheffield Medical School, U.K.
SOURCE: DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1998) 92 19-28. Ref: 54
Journal code: E7V; 0427140. ISSN: 0301-5149.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980625

AB Of the **vaccines** against **viral** diseases of man currently available, several are less than satisfactory, and the present surge of interest in improving such **vaccines**, and in developing new **vaccines** against **viral** diseases as yet unchallenged, has led to major developments in three areas. The capacity to identify the nature and form of **antigenic** epitopes in **proteins** allows the specific design of molecular entities to promote relevant and protective immune responses. Such entities, although ideal in terms of specificity and purity, may not achieve their goals through failure to reach relevant cells of the immune system due to simple dilution, elimination by host enzymes or **lack** of specific targeting. Concomitant with the above there has been development of a plethora of **adjuvants** aimed at enhancing immune responses to these 'new' immunogens, paralleled by an almost equally rapid increase in understanding the complex nature of the immune response, particularly with respect to **antigen** processing, the nature and role of cytokines and the importance of T-cell subsets in infection. These developments allow exploration of matching the properties and mechanistic action of a given **adjuvant** to a defined immune response. **Adjuvants** can be grouped according to their physical characteristics and mode of action. They include particulate **adjuvants**, oil and emulsifier-based **adjuvants**, those providing controlled **antigen** delivery, **adjuvants** based on specific targeting of **antigen**, and gel-type **adjuvants**. They may act non-specifically in promoting an immune response to an **antigen** through depot formation, or very specifically as in a "delivery system" where an **antigen** is linked to a cellular **protein**, targeted to a specific cell receptor. As **adjuvant** technology develops it is becoming increasingly clear that these differing approaches may be combined, and an **adjuvant**/delivery system designed, to provide slow release of a targeted **antigen**. The role of **adjuvants** in modern **viral vaccine** technology and their influence on the immune system are the subject of this review.

DOCUMENT NUMBER: 99401153 PubMed ID: 10469918
TITLE: **Positively charged** liposome functions as an efficient immunoadjuvant in inducing cell-mediated immune response to soluble **proteins**.
AUTHOR: Nakanishi T; Kunisawa J; Hayashi A; Tsutsumi Y; Kubo K; Nakagawa S; Nakanishi M; Tanaka K; Mayumi T
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Osaka University, 1-6, Yamadaoka, Suita, Osaka, Japan.
SOURCE: JOURNAL OF CONTROLLED RELEASE, (1999 Aug 27) 61 (1-2) 233-40.
Journal code: C46; 8607908. ISSN: 0168-3659.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991026
Last Updated on STN: 19991026
Entered Medline: 19991013

AB In order to design an optimized liposome immunoadjuvant for inducing cell-mediated immune response against soluble **proteinaceous antigens**, we investigated the effect of liposomal surface charge on the immunoadjuvant action. **Positively charged** liposomes containing soluble **antigens** functioned as a more potent inducer of **antigen**-specific cytotoxic T lymphocyte responses and delayed type hypersensitivity response than **negatively charged** and neutral liposomes containing the same concentrations of **antigens**. To clarify the reason of the differential immune response, we examined the delivery of soluble **proteins** by the liposomes into the cytoplasm of macrophages, using fragment A of diphtheria toxin (DTA) as a marker. We found that **positively charged** liposomes encapsulating DTA are cytotoxic to macrophages, while empty **positively charged** liposomes, DTA in **negatively charged** and neutral liposomes are not. Consistent with this, only macrophages pulsed with OVA in **positively charged** liposomes could significantly stimulate OVA-specific, class I MHC-restricted T cell hybridoma. These results suggest that the **positively charged** liposomes can deliver **proteinaceous antigens** efficiently into the cytoplasm of the macrophages/**antigen**-presenting cells, where the **antigens** are processed to be presented by class I MHC molecules to induce the cell-mediated immune response. Possible development of the safe and effective vaccine is discussed.



ACCESSION NUMBER: 96057687 MEDLINE
DOCUMENT NUMBER: 96057687 PubMed ID: 7551220
TITLE: Structure and properties of aluminum-containing **adjuvants**.
AUTHOR: Hem S L; White J L
CORPORATE SOURCE: Department of Industrial and Physical Pharmacy, Purdue University, West Lafayette, Indiana 47907, USA.
SOURCE: PHARMACEUTICAL BIOTECHNOLOGY, (1995) 6 249-76. Ref: 36
Journal code: BYR; 9310302. ISSN: 1078-0467.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 19951227
Entered Medline: 19951122

AB This chapter is concerned with the identification, characterization, and behavior of aluminum-containing **adjuvants** with **proteins** and anions similar to those occurring in vaccines and interstitial fluid. Aluminum-containing **adjuvants** referred to commercially as aluminum hydroxide have been identified as poorly crystalline aluminum oxyhydroxide with the structure of the mineral boehmite. Relevant properties of this material include its high surface area and its high pI, which provide the **adjuvant** with a high adsorptive capacity for **positively charged proteins**. Aluminum phosphate and alum-precipitated **adjuvants** may be classified as amorphous aluminum hydroxyphosphate with little or no specifically adsorbed sulfate. Variations in the molar PO4/Al ratio of amorphous aluminum hydroxyphosphates result in PI values that range from 5 up to 7; the materials are **negatively charged** at a physiological pH of 7.4. The amorphous nature of these compounds gives them high surface area and high **protein** adsorptive capacity for **positively charged proteins**. Observations on the interactions of anions and charged **proteins** with charged **adjuvant** surfaces have provided a framework for predicting behavior of complex systems of vaccines and for designing specific combinations of **adjuvants** and **antigens** to optimize the stability and efficacy of vaccines.

ACCESSION NUMBER: 84179455 MEDLINE
DOCUMENT NUMBER: 84179455 PubMed ID: 6713089
TITLE: The effect of surface charges of liposomes in immunopotentiation.
AUTHOR: Latif N; Bachhawat B K
SOURCE: BIOSCIENCE REPORTS, (1984 Feb) 4 (2) 99-107.
Journal code: A6D; 8102797. ISSN: 0144-8463.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198406
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19840607

AB The purpose of this study was to establish the effect of surface charges of liposomes on its **adjuvant** activity to an entrapped **protein antigen**. The immune responses of rabbits immunized subcutaneously with lysozyme entrapped in neutral negatively and **positively charged** liposomes and compared with complete Freund's **adjuvant** (CFA), showed **positively charged** liposomes to be a better **adjuvant** than neutral, **negatively charged** liposomes and even CFA. This was true for solid liposomes also. Interestingly, injection of **positively charged** liposomes led to the formation of granulomas at the sites of immunization, which was not observed with neutral and **negatively charged** liposomes.

L18 ANSWER 4 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998414931 EMBASE
TITLE: ISCOMs: An adjuvant with multiple functions.
AUTHOR: Sjolander A.; Cox J.C.; Barr I.G.
CORPORATE SOURCE: A. Sjolander, Immunology Department, CSL Limited, 45 Poplar Road, Melbourne, Vic. 3052, Australia. asjoland@csl.com.au
SOURCE: Journal of Leukocyte Biology, (1998) 64/6 (713-723).
Refs: 152
ISSN: 0741-5400 CODEN: JLBIE7
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Aluminum salts are currently the only widely used adjuvant for human vaccines. Over the past 10-15 years, a large research effort has attempted to find novel adjuvants with ability to induce a broad range of immune responses, including cell-mediated immunity. The immunostimulating complex or ISCOM is one adjuvant with multiple adjuvant properties. ISCOMs are open cage-like complexes typically with a diameter of about 40 nm that are built up by cholesterol, lipid, immunogen, and saponins from the bark of the tree Quillaia saponaria Molina. ISCOMs have been demonstrated to promote antibody responses and induce T helper cell as well as **cytotoxic** T lymphocyte responses in a variety of experimental animal models, and have now progressed to phase I and II human trials. This review describes recent developments in the understanding of the structure, composition, and preparation of ISCOMs and will cover important aspects of the understanding of the adjuvant functions of ISCOMs and how they act on the immune system.